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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/497,997	02/04/00	TERNYNCK	T 0660-0166-0X

HM12/0731

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EXAMINER	
BROWN, S	
ART UNIT	**PAPER NUMBER**
1648	15

DATE MAILED: 07/31/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/497,997	TERNYNCK ET AL.	
	Examiner	Art Unit	
	Stacy S Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *21-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 14, 16-17 and 20* is/are rejected.

7)☒ Claim(s) *6-15,18 and 19* is/are objected to.

8)☒ Claims *1-44* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 February 2000* is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4-5* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to **Group Art Unit 1648. Your application has been reassigned to examiner Stacy Brown.**

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-20, drawn to a polypeptide, classified in class 530, subclass 350.

II. Claim 21, drawn to the use of a polypeptide for preparing a composition intended to transfer substances into cells, classified in class 514, subclass 12.

III. Claim 22, drawn to the use of a polypeptide for the preparation of an antiviral composition, classified in class 435, subclass 69.7.

IV. Claims 23-31, 35-41 and 43-44, drawn to a polypeptide coupled to a substance, a vector and a cell, classified in class 435, subclass 320.1.

V. Claims 32-34 and 42, drawn to a method for transferring a substance into a cell, classified in class 435, subclass 455.

The inventions are distinct, each from the other because of the following reasons:

a) Inventions I and (II, III and V) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a

materially different process such as for preparing a composition intended to transfer substances into cells (Invention II), preparation of an antiviral composition (Invention III) and transferring a substance into a cell (Invention V).

b) Inventions I and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the polypeptide of Invention I is not disclosed as capable of use together with the polypeptide coupled to a substance. The polypeptide itself is used for delivery while the polypeptide coupled to a substance is used for delivery and treatment, therefore having different modes of operation, functions and effects.

c) Inventions II and III-V are unrelated. The method of use of a polypeptide for preparing a composition intended to transfer substances into cells does not share function, effect or outcome with the method of preparation of an antiviral composition (Invention III), nor a method for transferring a substance into a cell (Invention V). These methods are not disclosed as capable of use together. Invention IV, drawn to a polypeptide coupled to a substance and vaccine, is not disclosed as capable of use together with the method of preparing a composition intended to transfer substances into cells.

Further, if Group I is elected, applicant must elect one of SEQ ID NOS: 1, 2, 3 and 8. The sequences comprise different amino acids and have different lengths.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, and the literature and sequence

search required for one group is not required or co-extensive for any other group, restriction for examination purposes as indicated is proper.

During a telephone conversation with Daniel Pereira on 27 June 2001 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-20. Affirmation of this election must be made by applicant in replying to this Office action. Claims 21-44 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

3. Unfortunately, the not all of the references cited in form PTO 1449 were not received by the examiner. The US Patents and some of the non-patent literature were considered. Non of the foreign patent documents were received by the examiner or considered (no translations). Applicants are invited to resubmit the following references: Baccala et al and Sakano et al.

Drawings

4. The drawings are objected to by the Draftsperson, see PTO Form 948.

Specification

5. In Applicant's preliminary amendment (Paper No. 8), there is an amendment to the specification which contains an error. The instructions were to insert SEQ ID NOS on page 30, however the page should be page 36. Appropriate correction is required.

This application does not contain an **abstract** of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

6. Claims 6-15, 18 and 19 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other other multiple dependent claim. See MPEP § 608.01(n). Accordingly, claims 6-13, 15, 18 and 19 have not been treated further on the merits. *However, for the sake of compact prosecution the examiner has searched the various limitations in claims 6-13, 15 and 18 as best as could be determined in anticipation of applicant's amended claims. The rejections below will include various limitations of the improper multiple dependent claims, although the claims are not formally rejected.*

Claim 14 is objected to because it contains non-elected sequences.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5, 14, 16, 17 and 20 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a polypeptide having a unique or repeated peptide motif and comprising an amino acid sequence endowing it with the capacity to penetrate into cells. The polypeptide of the present invention is a product of nature. Suggested language is "isolated polypeptide".

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 14, 16, 17 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 recite "capacity to penetrate cells", which is indefinite because the word "capacity" means that the amino acid could penetrate cells, but may or may not actually do so.

Claim 16 recites the phrase "amino acid sequence capable of being obtained". This is indefinite because it is not clear whether or not the amino acid sequence is actually obtained. "Capable" means that it may or may not be obtained. Claim 17 recites "capable of" and is indefinite for the same reasons as claim 16. Claim 20 recites "capable of" and is indefinite for the same reasons.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-5 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by George et al (US Patent 5,861,156) and Kamireddy et al (US Patent 5,597,573) disclose methods of delivering agents to target cells, see abstract. Provided are single-chain antibody-peptide tag fusion proteins, comprising Fab and F(ab)'2 fragments, single-chain Fv (sFv) proteins and single-chain Fv fusion proteins, see column 2, lines 60-66. Fab and F(ab)'2 fragments encompass the hypervariable region, heavy chain, CDR2 and CDR3 regions of the antibody. **Although George et al do not specifically say that the antibody fragment is internalized into the cell, it is an inherent property of the antibody fragments disclosed.** Kamireddy et al teach that catalytic antibodies, such as IgG-type antibodies or catalytically active fragments thereof (Fab, Fv and single-chain antibodies) penetrate tissues better than ordinary antibodies, see column 4, lines 29-35.) Because of the inherent property of Fab, FV and single-chain antibodies of cellular penetration, George et al anticipate the instant invention.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1-5 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over George et al (US Patent 5,861,156) in view of Kamireddy et al (US Patent 5,597,573) and Curiel et al (US Patent 5,521,291). The claims are drawn to a polypeptide characterized by a unique or repeated peptide motif, and comprising an amino acid sequence endowing the polypeptide with the capacity to penetrate into cells and/or transport thereto a substance of interest. The amino acid sequence comprises one or more different antibody fragments, such as a portion of a hypervariable region, heavy chain antibody, or CDR3 region.

George et al disclose methods of delivering agents to target cells, see abstract. Provided are single-chain antibody-peptide tag fusion proteins, comprising Fab and F(ab)'2 fragments, single-chain Fv (sFv) proteins and single-chain Fv fusion proteins, see column 2, lines 60-66. Fab and F(ab)'2 fragments encompass the hypervariable region, heavy chain, CDR2 and CDR3 regions of the antibody. **George et al do not teach a polypeptide characterized in that the amino acid sequence is capable of being obtained by screening a peptide library for cell penetration. George et al do not teach a polypeptide characterized in that it comprises a polylysine region.**

It would have been obvious to one of ordinary skill in the art at the time the invention was made, to use the method of screening a peptide library for desired activity because it is a well known method, as evidenced by Kamireddy et al, see column 9, lines 3-6. One would have been motivated to do use the library screening method because Kamireddy et al use the same method to screen for catalytic antibody activity (antibody penetration). It would have been obvious to modify George et al by adding a polylysine region to function as an internalizing factor, as taught by Curiel et al, which discloses conjugates of virus and antibody for transporting gene constructs into high eucaryotic cells. One would have been motivated to modify the polypeptide of George et al to incorporate a polylysine region for additional internalizing potential because Curiel et al teach that the polylysine region has affinity for nucleic acid and is useful for directing their virus-conjugated-antibody into cells, see abstract and columns 14-15. One would have had a reasonable expectation of success that such modifications would be effective for screening for a polypeptide and for internalization into a cell because Kamireddy and Curiel teach screening of penetrating antibodies and penetration into cells by such methods. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention as made.

Conclusion

11. Claim 14 is free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy S Brown whose telephone number is 703-308-2361. The examiner can normally be reached on M-F and alternate W (7:30-4:00 EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Stacy Brown
July 27, 2001

HANKYEL T. PARK, PH.D
PRIMARY EXAMINER